Applicants respectfully traverse the 35 U.S.C. § 112, first paragraph rejection of Claims 20, 31, 33 to 36 and 41. The specification as filed sufficiently enables one skilled in the art to use the invention commensurate with the scope of Claims 20, 31, 33 to 36 and 41. Applicants specifically refer the Examiner to page 9, line 12 to page 10, line 17, which is reproduced below:

> One skilled in the art can readily identify patients in need of treatment for preventing, delaying or reversing the progression of Alzheimer's Disease. Clinical symptoms of AD include, for example, progressive disorientation, memory loss, and aphasia. Eventually, disablement, muteness, and immobility occur. Pathological indicators of AD include, for example, the presence of neurofibrillary tangles, neuritic plaques, and amyloid angiopathy. Preventing the progression of AD means preventing the onset or further development of clinical symptoms and/or pathological indicators of AD. For example, an individual who does not have clinical symptoms or pathological indicators of AD can be prevented from developing clinical symptoms or pathological indicators. Further, an individual who has a mild form of AD can be prevented from developing a more severe form of AD. Delaying the progression of AD means delaying the time of onset of AD-related symptoms and/or pathological indicators or slowing the rate of progression of AD, determined by the rate of development of clinical symptoms and pathological indicators. Reversing the progression of AD means lessening the severity of an AD condition, i.e., the AD condition of an individual has changed from severe to less severe as indicated by fewer clinical symptoms or pathological indicators.
>
> An individual can choose to take an Aβ42 lowering agent as a preventative measure to avoid developing AD. For example, an individual with a genetic predisposition to AD can take an Aβ42 lowering agent to prevent or delay the development of AD. A genetic predisposition can be determined based on known methods. For example, an individual can be considered to have a genetic predisposition to AD if the individual has a family history of AD. Genetic predisposition to AD also can include point mutations in certain genes such as the APP gene, the presenilin-I or presenilin-2 gene, or the apolipoprotein E gene. Such mutations can predispose individuals to early-onset familial AD (FAD), increased risk of developing AD, or decreased age at onset of AD. (See page 1332, Table 30-2 of Cotran et al. (1999) *Robbins Pathologic Basis of Disease*, Sixth Edition, W.B. Saunders

> Company; and U.S. Pat. No. 5,455,169.) Furthermore, an individual who has clinical symptoms of, or has been diagnosed with, AD can take an Aβ42 lowering agent to prevent or delay further progression of AD as well as to reverse the pathological condition of the disease.
>
> An AD diagnosis can be made using any known method. Typically, AD is diagnosed using a combination of clinical and pathological assessments. For example, progression or severity of AD can be determined using Mini Mental State Examination (MMSE) as described by Mohs et al. (1996) *Int Psychogeriatr* 8:195-203; Alzheimer's Disease Assessment Scale-cognitive component (ADAS-cog) as described by Galasko et al. (1997) *Alzheimer Dis Assoc Disord,* 11 suppl 2:S33-9; the Alzheimer's Disease Cooperative Study Activities of Daily Living scale (ADCS-ADL) as described by McKhann et al. (1984) Neurology 34:939-944; and the NINCDS- ADRDA criteria as described by Folstein et al. (1975) *J Psychiatr Res* 12:189-198. In addition, methods that allow for evaluating different regions of the brain and estimating plaque and tangle frequencies can be used. These methods are described by Braak et al. (1991) *Acta Neuropathol* 82:239-259; Khachaturian (1985) *Arch Neuro* 42:1097- 1105; Mirra et al. (1991) *Neurology* 41:479-486; and Mirra et al. (1993) *Arch Pathol Lab Med* 117:132-144.

As stated above, one skilled in the art can readily identify patients in need of treatment for preventing, delaying or reversing the progression of Alzheimer's Disease. Once identified, an Aβ42 lowering agent can be administered to the patient to prevent, delay or reverse the progression of Alzheimer's Disease as defined above. Thus, the specification enables one skilled in the art to use the invention without undue experimentation.

Applicants respectfully submit the Examiner is requiring an overly strict test for enablement. Page 5 of the Office Action states the test as follows:

> In order to prevent a disease, one would need to precisely identify those subjects likely to acquire such a disease, administer Applicant's claimed invention, and *then demonstrate that if the identified subject did not develop the disease, such an effect was the direct result of the claimed invention* (emphasis added).

The first two parts of the test are clearly within the ability of one skilled in the art. As stated in the Specification, one skilled in the art knows how to identify patients in need of treatment for preventing, delaying or reversing the progression of Alzheimer's Disease. One skilled in the art clearly knows how to administer a compound to a patient at the appropriate dose. *See* M.P.E.P. § 2164.01(c). Applicants disagree that enablement requires the Applicant to "demonstrate that if the identified subject did not develop the disease, such an effect was the direct result of the claimed invention." Even for treatment claims, it may not be possible to conclude that the treatment of the disease was the direct result of administration of the compound. For example, when a patient suffering from pain is administered an analgesic, one skilled in the art could not conclude with absolute certainty that the pain relief was the direct result of the analgesic. It is always possible that the pain could have subsided without the analgesic. The Examiner is pronouncing an impossible standard that can never be met for patenting a prevention claim. The Examiner's test is such a high standard that it essentially excludes such claims from patent protection in all cases. Clearly, prophylactic treatment is common in the medicinal arts and patent protection for such methods should be allowable.

Moreover, Applicants refer the Examiner to Veld, et al., N Eng J Med, Vol. 345, No. 21, pp. 1515-1521 ("Veld"), submitted with the Information Disclosure Statement dated June 23, 2005. Veld teaches that the long term use of NSAIDs has a beneficial effect on the risk of Alzheimer's. *See* Table 3. Veld evidences the prevention of Alzheimer's disease is well within the knowledge and purview of one skilled in the art.

Applicants respectfully submit that the application is in condition for allowance and passage thereto is earnestly requested. This Amendment is accompanied by an information disclosure statement. The Commissioner is authorized to charge the fee required for the information disclosure statement under 37 C.F.R. 1.17(p) to Merck Deposit Account No. 13-2755. Any additional fees required in connection with this Amendment or the information disclosure statement may be taken from Merck Deposit Account No. 13-2755. The Examiner is invited to contact the undersigned attorney at the telephone number provided below if such would advance the prosecution of the case.

Respectfully submitted,

By _____

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